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New Advancements in the Field of Optical Sensors (WGM and SPR)

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Abstract: Due to its ability to identify the presence of the label-free molecule as a result of a change in the medium's or analyte's refractive index, optical biosensors are now regarded as transducers. These opticalbased sensors can quickly identify any alteration in the optical characteristics of the detecting medium. For instance, surface plasmon resonance (SPR) based Photonic crystal fibres, microsphere resonators and Mach-Zehnder interferometers. The rapid advancement of genetics and biochemistry has made it possible to identify numerous diseases with extraordinary accuracy by expanding the range of medical and biological tools. Due to the many properties of absorption, transmission, and reflection of light waves for the change in the surrounding medium, optical-based sensing currently dominates in biosensors. The Whispering Gallery Mode (WGM) concept is a popular choice among these optical sensors for use in bio-sensing. Optical sensor technology has been transformed by whispering gallery modes (WGM). The design and simulation of a unique "multi-core whispering gallery mode (WGM)" for the detection of cancer cells is given. This structure is based on multiple evanescent waves coupling. A finite element method-based simulation tool was used to complete the comprehensive simulation portion of this work. Our simulation predicts already published elsewhere that the suggested sensor had a sensitivity of 650 nm/RIU, 666.67 nm/RIU, and 642.285 nm/RIU for the detection of malignant Basal, HeLa and MDB-MB-231 cells, respectively. To the greatest extent of our understanding, the suggested sensor's sensitivity is likely the highest among WGM-based bio-sensors used up to this point.

With the biological or chemical analyte in close contact with the sensor metal layer, Surface Plasmon Resonance (SPR) phenomenon is a relatively new and extremely sensitive technology for detecting refractive index variation. Even though there are currently a number of SPR-based biosensors on the market, researchers are keen on increasing the sensors' sensitivity and exposing them to a variety of spectrum for sensing applications. Surface plasmon (SP) oscillations, which are free electron oscillations, provide the basis for the SPR-based sensor's operation. The SP mode is excited by p-polarized light entering the prism (BK7), and by applying the angular interrogation technique, the resonance or SPR angle (θ spr) has been estimated by analyzing the output reflectance (%) line. The output reflectance intensity of the light wave (%) degrades from the intensity of the incident light wave as a result of the multilayer interfaces. However, in the SPR resonating state, the reflectance intensity (%) becomes minimal (Rmin)

because the surface plasmons are most intensely excited. A graphene-coated surface plasmon resonance (SPR) based biosensor for focusing on particular biological components was designed and simulated by Shahriar et al. in their article published in 2021. By employing a numerical simulation on the finite element technique (FEM), they explicitly demonstrated how to detect the amount of haemoglobin in blood samples and the level of glucose concentration in urine samples. Using this SPR-based sensor with 200 deg/RIU angular sensitivity, it has been determined that the 0.001 refractive index increment in the blood component results in an increase in haemoglobin (HB) levels of 6.1025 g/l. Additionally, they used this SPR sensor to determine if diabetes is present or absent based on the glucose concentration level in urine samples. **Keywords:** WGM, SPR, optical sensor.

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Recent Advances in Silicon Photomultipliers: Enabling New Biophotonics Discoveries and Technologies

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Abstract: Time resolved methods in biophotonics are rapidly advancing since the emergence of new Silicon photomultiplier (SiPM) -based technologies which can be operated in Geiger mode facilitating a wide variety of applications from cancer therapeutics to optical biomodulation of organisms, to bioenvironmental analysis. Silicon photomultiplier detectors provide several advantageous features over traditional photomultiplier tubes combining highly sensitive photon counting with miniaturized and ruggedized packaging, low voltage operation, immunity to magnetic field interference, and low-cost detection. We present here our recent advances in the opto-electronic design, development and deployment of new, portable, time-domain single photon counting biosensor devices, cable of capturing ultra-low intensity light emissions from biological materials and specimens using a SiPM. We will discuss a range of promising new biophotonics probes integrating these solid-state single-photon avalanche diode arrays, from environmental surveillance of plant photosynthetic disruption due to temperature induced stress, to examining acousto-optic stimulation of bioluminescence in single cell organisms, to high speed-pump-probe technologies for interrogation of the pO2 micro-environment in cancer- useful in understanding tumorogenesis and engineering new molecular dosimetry techniques in photonic cancer therapies. **Keywords:** time-resolved bioluminescence, molecular PO2 biosensing, delayed fluorescence, Geiger

mode single photon counting, silicon photomultiplier (SiPM).

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Mechatronic Systems for Vibration Control in Laser Medical Instruments

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Abstract: The paper analyzes the problem of vibrations in portable laser equipment, occurring mainly due to hand tremor, and proposes mechatronic compensation solutions, both semi-active and active. Not observed during daily life activities, tremor - in all its forms, can have an impact on one's life. The most relevant examples where tremor is mentioned are the imaging sessions (CT, MRI) where it can alter the procedure result. Tremor is an unvoluntary, oscillatory and rhythmic movement which is produced by reciprocally innervated antagonist muscles. Small amplitude tremor which comes together with normal posture and movement is called physiologic tremor. There are many devices specially created for hand tremor compensation based on different levels of tremor amplitude varying from hand shaking disorders to physiological tremor. Different suppression methods of pathological hand tremor may consist in special hand tools designed with an active cancelling actuating system. These devices are critical in special medical procedures such as brain tumor removal and ophthalmological microsurgery. One example of a handheld active tremor compensation instrument is called Micron. The first iteration of Micron used piezoelectric actuator to position the tip of the instrument, independently of the body, controlled by a visual feedback loop (a LED attached to the tip and a PSD – Position Sensing Detector). Second iteration of Micron used an accelerometer to detect the tip movement and to estimate the hand tremor. Another mechatronic device for microsurgeries uses bimorphs actuators and an IMU to position the instrument tip. There are some examples based on micromotors connected into a Gough-Stewart platform configuration which provides six degrees of freedom and allow the device to position the tip efficiently and compensate the tremor on all DOF.

This article studies possible solutions to compensate for hand movement in order to stabilize the position of the laser beam on the surface and to correct defocusing. From the analysis of the operation of such systems several possible solutions were identified, based on optical or mechanical solutions. The purely mechanical solution is based on the grouping of the entire optical system (source, collecting/collimating lens and the focusing lens) in a single assembly and its displacement in space. The practical solution is to create an actuation system with integrated compliant support system. The actuation could be based on electromagnetic, electrodynamic or piezoelectric actuators. The optical solution is based on moving the focus lens, on using Risley prisms or using a set of deflection mirrors. Both solutions are studied from the

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point of view of design and performances. Finally, a mechanical solution with laser diode displacement using a modified Stewart platform type mechanism and optical solutions with mirrors placed on piezoelectric actuators is presented and with focusing lens displacement. The problems of signal acquisition and processing and control optimization are also discussed.

Keywords: Vibration control; tremor; laser micro-surgery; opto-mechatronic systems; optical stabilization. **Acknowledgement:** This work was supported by a grant of the Romanian Ministry of Education and Research, CCCDI-UEFISCDI, project number PN-III-P2-2.1-PTE-2019-0253, within PNCDI III.

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Role of Non-Invasive Optical Neuromonitoring in Brain Function and Injury Assessment

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Abstract: The past two decades have seen the growing importance given to optical technologies deployed in providing measures of cognitive functioning and brain health in real time, under ecologically valid conditions as well as in field settings. Understanding the inner workings and functional make-up of the human mind and monitoring the individual's current neurophysiological state by properly adapting these optics-based neuroimaging methodologies, can guide clinicians, scientist and researchers in improving the diagnosis, treatment and prevention of brain disorders and injuries. As such, near-infrared spectroscopy (NIRS) is an emerging optical neuroimaging technology that holds untapped potential for clinical use and research applications that require real world and real time brain imaging adaptable to more complex and dynamic environments. The technology uses near-infrared (NIR) light to assess changes in blood oxygenation and volume in the cerebral cortex and allows the design of safe, portable, wearable, noninvasive, and affordable neuromonitoring systems with rapid application time, superior immunity to movement noise, and near-zero run time cost. This talk will introduce the principles underlying NIRS technology, sensor development and evolution, its data analytics using novel signal processing algorithms on innovative physical and digital head model designs, animal and human tests, in the field studies and clinical evaluations. Special focus will be given to both functional and physiological neuromonitoring applications on attention and memory processing, cognitive aging, learning, training and cognitive enhancement, and traumatic brain injury assessment.

Keywords: optical brain imaging, near infrared spectroscopy, cognitive activity monitoring, brain injury detection, phantom, animal and human testing.

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Comparative Analysis of Radiation Response in Chemo-Treated BT20, 4T1 Breast Cancer, and Neuroblastoma Cancer Cell Lines through Single and Multiple Cell Ionization Using Infrared Laser Trapping

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Abstract: The aim of our study was to use laser trapping technique to evaluate the radiation sensitivity of cancer cells, both untreated and chemo-treated. We focused on a specific human breast tumor cell line, called BT20, that was treated with an antitumor compound known as 2-Dodecyl-6-methoxycyclohexa-2, 5-diene-1, 4-dione. We investigated an untreated control group, as well as two groups of BT20 cells that were subjected to different treatment durations. We utilized a high-power infrared laser (at 1064 nm) trap to determine the absorbed threshold ionization energy (TIE) and threshold radiation dose (TRD) for single and multiple cells trapping and ionization. We performed statistical analyses, including descriptive and one-way ANOVA, on the results. We also analyzed the relationship between TIE and TRD to the mass of the individual cells for different hours of treatment, in comparison to the control group. Our findings revealed that both TIE and TRD decreased as treatment duration increased. However, the TRD decreased with mass irrespective of the treatment. Moreover, our analyses consistently showed the same behavior of TRD for single vs. multiple cell ionizations within each group, regardless of treatment. In addition, we conducted a comparative analysis on the effects of radiation dosage in BT20, 4T1 breast cancer, and N2a neuroblastoma cell lines, and discovered that the TRD decreased in mass across all three cell lines. **Keywords:** Breast cancer cells, laser trapping, cell mechanics, chemotherapy, radiotherapy.

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Advancing Optical Coherence Tomography Probes for Multidimensional Intracorporeal Imaging

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Abstract: Optical Coherence Tomography (OCT) has emerged as a potent nondestructive modality for high-resolution imaging of tissue microstructures in depth. In its initial utilization, OCT found application in organs such as the retina and skin, benefiting from their direct accessibility through conventional optical pathways. However, the innate limitation in penetration depth necessitated innovative strategies to extend OCT's reach into deeper anatomical regions, leading to the integration of fiber optics and endoscopic approaches.

In the upcoming presentation we aim to impart a condensed yet comprehensive account of our extensive and profound experience spanning close to a quarter-century. Our scope spans from coronary arteries to the gastrointestinal tract, lungs, biliary tree, brain, and virtually every other facet of the human body. Through adept utilization of endoscopes, catheters, and needles, we have navigated the complexities of diverse anatomical landscapes, harnessing the potential of OCT to illuminate intricate tissue structures.

In addition, we are excited to introduce the latest advancements within our field during the presentation. Despite the time constraints, we are committed to providing an overview of these cutting-edge developments that reflect the ever-evolving landscape of Optical Coherence Tomography (OCT). Our intent is to offer insights into the novel techniques, technologies, and methodologies that are reshaping the boundaries of intracorporeal imaging. By incorporating these recent breakthroughs, we seek to underscore the ongoing innovation that continues to drive the potential of OCT to new heights.

Keywords: OCT; fiber optics; catheters; probes; imaging.

Acknowledgement: This research was conducted at Wellman Center for Photomedicine at Massachusetts General Hospital supported by the Center and grants from NIH.

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Rapid Characterization and Detection of Extended-Spectrum β-Lactamase-Producing Bacteria Isolated Directly from Urine by Infrared Spectroscopy and Random Forest

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Abstract: Over the past few decades, the emergence of antibiotic-resistant bacteria has become a prominent global concern. Notably, bacteria that produce Extended-Spectrum β -Lactamases (ESBL), including prevalent species such as E. coli and Klebsiella (K.) pneumoniae, constitute a noteworthy category within the realm of antibiotic-resistant infectious bacteria. As ESBL-producing (ESBL+) resistant bacteria continue to evolve, numerous commonly used antibiotics have lost their efficacy against them. The development of a rapid and reliable detection method for ESBL+ bacteria will improve the efficiency of treatment and limit the dissemination of these isolates.

In this study, we investigated the capability of infrared spectroscopy-based Random Forest for the instant detection of ESBL+ bacteria isolated directly from patients' urine. The investigation encompassed 1881 E. coli samples (416 ESBL+ and 1465 ESBL-) and 609 K. pneumoniae samples (237 ESBL+ and 372 ESBL-), all isolated directly from midstream urine specimens. Our results revealed that within 40 minutes of receiving the patient's urine, it is able to identify the infecting bacterial species with 95% accuracy and detect ESBL+ E. coli and K. pneumoniae at rates of 83% and 78% accuracy, respectively.

Keywords: E. coli, klebsiella pneumoniae, ESBL, infrared microscopy, machine learning.

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Label Free Detection of the Structure below the Resolution Limit of the Imaging System

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Abstract: At high resolution, a microscope's field of view is commonly much smaller than the sample region of interest. Pathologists examining suspected tumor sections overcome this limitation by translating the section. Biologists assessing the extent of mitosis (cell division) in a cell population undertake a more quantitative analysis, laboriously examining multiple images that cover the region of interest. We investigated a few approaches, including digital Fourier holography, spectral encoding of spatial frequency (SESF) microscopy and nano-sensitive optical coherence tomography (nsOCT) to accomplish them much more efficiently. Common features of our approaches include the use of simple, low-numerical aperture optics, giving a wide field of view and long working distance, and analysis of the angular or spectral distribution of the scattered light to extract the microscopic information with nano-sensitivity to structural alterations.

Keywords: Biomedical optics; label free imaging; optical coherence tomography; nano-sensitivity; submicron structure; depth resolved imaging.

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Application of Infrared Spectroscopy in Conjunction with Machine-learning for Rapid Assessment of Bacterial Susceptibility to Antibiotics

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Abstract: Bacterial infections claim over 6.7 million lives annually, ranking as a primary global cause of human illness and death. The primary treatment for such infections is antibiotics, but the surge in bacterial resistance to commonly used antibiotics has led to untreatable infections. One significant contributor to this resistance increase is the extended period, approximately 48 hours, required for traditional methods to determine bacterial susceptibility to antibiotics. This extended delay has resulted in random and excessive antibiotic use, fostering the emergence of multidrug-resistant bacteria.

Fourier-transform infrared (FTIR) spectroscopy offers a rapid and sensitive approach capable of detecting subtle molecular alterations within cells, particularly those linked to antibiotic resistance development. The primary objective of our proposed research is to assess the potential of FTIR spectroscopy in conjunction with machine learning algorithms to promptly determine bacterial susceptibility to various antibiotics within approximately 30 minutes after initial culture.

We conducted extensive measurements and analyses on thousands of samples utilizing various machine learning algorithms. Our findings demonstrate that it is possible to determine the susceptibility of diverse bacterial species to various antibiotics with an accuracy exceeding 80%.

Keywords: Bacterial infections, multi-drug resistance, antibiotic susceptibility, infrared microscopy, machine learning.

POSTER PRESENTATION

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Vision Improvement by Dynamic Optics

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Abstract: Vision provides a majority of information that the brain needs to perceive the world. Simple defocus, which deteriorates vision, can be corrected with conventional lenses. Nevertheless, more complicated defects, such as irregular astigmatisms, cannot be compensated with conventional ophthalmic lenses and require more specific and advanced methods to be corrected. To meet these needs, we designed and constructed a VIDO (Vision Improvement by Dynamic Optics) device. It virtually places any optical element designed for eye correction as a contact lens or IOL, enabling objective and subjective determination of the quality of vision with a possibility of a feedback loop. The valuable issue of VIDO technology is so-called open-field functioning. After virtual correction patient could look through the device to see standard far-vision charts or natural scenes in the room. Devices currently available in the world's markets do not provide natural sight testing capability. Such functionality is valuable, especially in the prospect of suppression of high-order aberrations or testing new correction methods. The VIDO device allows also testing such elements projected on the patient's eye's cornea without the need for expensive manufacturing of single units of experimental correction elements. We offer the VIDO device that virtually places any optical element designed for eye correction as a contact lens or an intraocular lens (IOL), enabling objective and subjective determination of the quality of vision with a possibility of a feedback loop. Keywords: vision; optometry; adaptive optics; presbyopia; virtual correction.

Acknowledgement: The research was supported by the National Center for Research and Development under the LIDER program (LIDER/15/0061/L-9/17/NCBR/2018).

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POSTER PRESENTATION

ld-3

Analysis of Performance of Light Sword Lens on Retina of a Human Eye

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Abstract: Light Sword Lens (LSL) is positively validated as a correction method for presbyopia, which manifests in loss of accomodation of the eye. Until now, the research focused on paraxial regime of imaging with a simplified eye model and flat image surface, while in reality the eye is much more complicated optical system consisting of few optical interfaces and a curved retina. Moreover, the numerical analysis used LSL as a diffractive element and the imaging was simulated using scalar diffraction theory. To address this issues, we propose a new and more thorough method of analysis of performance of the LSL. We used the well-known method of ray tracing in an optical setup consisting of the LSL element implemented as a contact lens and a realistic Navarro eye model. This allows to assess the imaging properties of the whole eye with the LSL contact less applied, including non-paraxial imaging regime. This is very important as human vision extends beyond paraxial regime. Moreover, optical properties of human eye, such as aberrations, can influence performance of the LSL element in a previously unknown manners. The results give significant insight into working of LSL and human eye as a whole and will allow for applying modifications to the element in order to improve quality of patient's vision.

Keywords: Light sword lens; vision; eye model; presbyopia; contact lens.

Acknowledgement: The research was supported by the National Center for Research and Development under the LIDER program (LIDER/15/0061/L-9/17/NCBR/2018) and by Warsaw University of Technology (Scientific Council for Physical Sciences grant)

POSTER PRESENTATION

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Early Detection of Herpetic Infections using FTIR Spectroscopy

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Abstract: Herpes viruses are responsible for a variety of mild to severe human diseases, which are sometimes life-threatening, particularly in immune-comprised patients. After the acute infection, herpes viruses establish latency and persist in different cells of the body, according to the infecting virus, for a lifetime. Rapid identification of herpes infection is crucial for successful treatment. The conventional techniques employed to detect herpes infections are time-intensive. FTIR spectroscopy, on the other hand, offers a sensitive and dependable approach capable of discerning subtle molecular alterations. Thus, the main aim of this study is to assess the potential of utilizing microscopic FTIR spectroscopy as a highly sensitive method for early-stage detection of herpetic infections. Our findings revealed noteworthy and consistent distinctions among all examined normal cells and those infected with either HSV or VZV. Discernible and substantial spectral differences between normal and infected cells emerged as early as 24 hours post-infection, while observable cellular damage (cytopathic effect) attributable to the infecting virus was only evident through optical microscope observations at the 3-day mark following infection. Additionally, there was a remarkable upswing in the levels of crucial cellular metabolites observed in cells infected with herpes viruses when compared to their normal cells. The distinctive spectral behavior we observed appears to be exclusive to herpes virus infections. When these cells were exposed to viruses from unrelated families, such as retroviruses, different spectral changes were obtained compared to those received with cells infected with herpes viruses. Employing cluster analysis on FTIR spectroscopy data resulted in a 100% accuracy rate in distinguishing between control uninfected cells and those infected with VZV or HSV. Our findings robustly endorse the potential of FTIR microscopy as a diagnostic tool for early herpetic infection detection.

Keywords: Viral infections, VZV, HSV, infrared microscopy.

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